INTRAVENOUS LIPID EMULSION FOR THE TREATMENT OF PERMETHRIN TOXICOSIS IN CATS

by

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This thesis is presented for the degree of

Research Masters with Training (Veterinary Medical Science) of Murdoch University

2014

I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary institution.

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Abstract

Over the last decade, a growing interest has emerged in the use of intravenous lipid emulsions in the treatment of lipophilic drug toxicoses. Initial interest in the therapy was prompted by its successful use in rats and dogs for reversing the life-threatening cardiovascular effects of local anaesthetic overdoses. A postulated mechanism of action of intravenous lipid emulsion in lipophilic drug toxicoses is lipid partitioning, which is creation of an intravascular lipid compartment into which lipophilic drugs may be bound and sequestered away from their sites of action. Permethrin is a highly lipophilic insecticide which can cause significant morbidity and mortality in cats through its neuroexcitatory effects. Permethrin is a common ingredient in flea treatments marketed for dogs and accidental administration to cats is common. The aims of this study were to (1) determine if a lipid emulsion added to permethrin-containing feline plasma *in vitro* would lead to a decrease in plasma permethrin concentration thus supporting a lipid sink effect, and (2) assess the clinical response to intravenous lipid emulsion administration in cats with permethrin toxicosis. In the *in vitro* study, addition of a lipid emulsion to permethrin-containing feline plasma led to a significant reduction in plasma permethrin concentration within 30 minutes. In the clinical trial, there was a significant difference in the distribution of clinical stages over time between treatment groups, with cats receiving 20% intravenous lipid emulsion having lower clinical stages earlier than cats receiving the saline control. The results of these studies support the use of intravenous lipid emulsion in the treatment of permethrin toxicosis in cats and the *in vitro* study supports intravascular lipid partitioning as a mechanism of action. Future research is needed to confirm lipid partitioning as a mechanism of action of intravenous lipid emulsion *in vivo* for lipophilic drug toxicoses, determine the metabolic fate of lipid sequestered drugs and

ascertain adverse effects of intravenous lipid emulsion at the doses recommended for drug toxicoses.

Acknowledgments

The author would like to thank Associate Professor Robert Trengove and Mr Bruce Peebles from the Murdoch University Separation Science Laboratory for their contribution in determining the permethrin concentrations of the samples for the *in vitro* study reported in this thesis, and Dr Katrin Swindells from Western Australian Veterinary Emergency and Specialty for her input into study design for the clinical trial.

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